Acute Grass Disease: GREIG, J

An Interpretation of the Clinical Symptoms.

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PAPER

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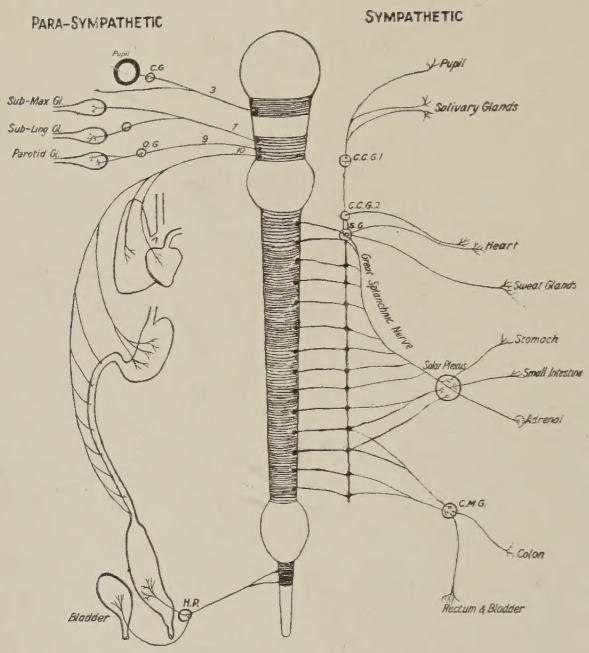

PARA-SYMPATHETIC.	SYMPATHETIC.
C.G. Ciliary Ganglion.	C.C.G.1. Cranial Cervical Ganglion.
O.G. Otic Ganglion.	C.C.G.2. Caudal Cervical Ganglion.
H.P. Hypogastric Plexus.	S.G. Stellate Ganglion.
3, 7, 9, 10. The figures refer to the Cranial Nerves.	C.M.G. Caudal-mesenteric Ganglion.

Scheme of the general arrangement of the Autonomic Nervous System, the distribution of Sympathetic and Parasympathetic portions being contrasted on the two sides of the diagram. (Partly after Langdon Brown).

Acute Grass Disease.

An Interpretation of the Clinical Symptoms.

In investigating the cause of an obscure epizoötic it may be profitable to study the effects which the disease produces upon the functions of the organs as well as upon their structure.

The evidence furnished to the pathologist on a post-mortem examination of the cadaver may be important enough, but valuable clues to the nature of the disease may emerge from a close study of these signs of disordered function which we call clinical symptoms. Although the pathologist encounters the conditions which have caused death, it does not always follow that such conditions can be accepted as manifestations of the *nature* of the disease. In other words, those signs which result from the early, as distinct from the ultimate effects of disease may, in their proper interpretation, furnish us with important information as to the origin of the pathogenesis.

In Acute Grass Disease we are furnished with a clinical picture composed of definite symptoms, and, although in individual cases this or that symptom may be represented in varying degrees of intensity, the picture is essentially the same in the details of its composition.

For reasons which will appear later, there seems good cause for believing that the symptoms in the acute type represent the effects of functional nervous derangement, and, before proceeding further, it would be well to glance at the structure and function of the Central Nervous System.

The nerve fibres which compose the conducting mechanism of the Central Nervous System fall into two main groups :—

(1) *Afferent fibres* which conduct messages from all parts of the body to the Central Nervous System.

(2) *Efferent fibres* which conduct messages from the brain and cord to the peripheral parts of the body.

Efferent nerve fibres may be primarily classified as :—

(*a*) those which innervate voluntary muscle and are therefore under the governance of the will, and concerned in voluntary movement.

(*b*) those which govern the processes of the body over which there is no voluntary control.

The vital processes, such as cardiac contraction, gland secretion, intestinal movement, etc. are not under the control of the will and represent a system of self government or autonomy, and the nervous mechanisms which control such functions form what is known as the Autonomic Nervous System.

The Autonomic Nervous System includes two distinct mechanisms :—

(1) The PARASYMPATHETIC, composed of

(*a*) fibres issuing from the brain stem in the 3rd, 7th and 9th cranial nerves, together with all the efferent fibres in the 10th cranial nerve (Cranial Autonomic).

(*b*) fibres issuing from the anterior roots of certain sacral nerves (Sacral Autonomic).

(2) The SYMPATHETIC, which originates in fibres given off from the cord in the anterior roots of the spinal nerves between the cervical and sacral swellings.

These two systems, the Parasympathetic and the Sympathetic are mutually antagonistic since, in the main, the effects produced by their respective stimulation are opposed ; thus, while the Parasympathetic is motor to the intestine, the Sympathetic inhibits its peristaltic movement ; the Parasympathetic inhibits the heart's action ; the Sympathetic accelerates it. It is by this process of counteraction that a condition of "balance" in the vital functions is largely maintained.

The effects produced by the respective stimulation of the Parasympathetic and Sympathetic systems may be briefly shown in the following table :—

TABLE No. 1.

AUTONOMIC NERVOUS SYSTEM.

PARASYMPATHETIC.		SYMPATHETIC.
Contract	Pupil	Dilate
Inhibit	Heart	Accelerate
Secrete (thin and watery)	Salivary Glands	Secrete (thick and glairy)
Motor	Stomach	Inhibit
Nil	Pyloric Sphincter	Constrict
Motor	Intestines	Inhibit
Nil	Ileo-Cæcal Sphincter	Constrict
Contract	Bladder	Relax
Nil	Sweat Glands	Secrete
———	Superficial Muscles	Tremor
Nil	Voluntary Muscles Generally	Increased Plastic Tonicity
Constrict	Bronchi	Relax
Nil	Anal Sphincter	Constrict

The condition of balance which is maintained by the counteraction of these two systems may be upset by various factors which elicit a specific effect of stimulation

or depression on one or other of the divisions of the Autonomic Nervous System. These factors include such varied substances as vegetable alkaloids, toxins and endocrine secretions. Thus :—

Arecoline Physostigmine Pilocarpine Acetyl-choline	Stimulate Parasympathetic.
Atropine Hyoscyamine	Depress Parasympathetic.
Adrenaline Tyramine	Stimulate Sympathetic.
Ergotamine	Stimulates, but later depresses Sympathetic (motor fibres).

Certain agents, then, are known to excite one or other of the systems, and in so doing they produce a condition of *relative* depression in the opposite system. Conversely, those agents which depress one system produce a condition of *relative* activity in the other.

A condition of dominance in the Parasympathetic is spoken of as VAGOTONIA, while SYMPATHICOTONIA is used with reference to excessive activity of the Sympathetic.

Grass disease occurs in acute, sub-acute and chronic forms, and, in the present state of our knowledge, all three forms are generally regarded as representing differing degrees in the manifestation of one essential pathological condition.

In a study of the symptomatology, such as one is here attempting, the acute form alone will be considered, because in the more chronic types secondary symptoms develop which make for confusion and so obscure the issue.

As has already been indicated, acute grass disease is remarkable in that it is always presented clinically as a definite and complete syndrome ; that is to say, its recognised clinical symptoms are practically always present (although in variable degree), in all cases.

In the acute form there is little or no fever ; the pulse is accelerated ; a variable amount of thick glairy saliva is secreted ; there is difficulty in swallowing, and regurgitation of ingesta may occur ; the intestines are in a condition of stasis which approaches the absolute ; there is frequently retention of urine ; sweating and the development of fine muscular tremors are also observed ; there is increased muscular tonus which may amount to tonic contraction, especially in the lumbar and gluteal groups (this is evidenced by the impression of hardness or "resistance" obtained by digital palpation) ; the sphincters of the alimentary tract are in tonic spasm.

This last statement may require some explanation. The spasm of the *Pyloric Sphincter* is evidenced by the acute distension of the stomach with fluid. Further, it has been observed by Nairn (private communication), that large doses of strychnine, if administered by mouth, produce no toxic effects in acute grass disease ; the strychnine being presumably confined to the stomach and its absorption by the small intestine thus prevented.

Spasm of the *Ileo-Cæcal Sphincter* is shown by the sudden and sharp change in the nature of the intestinal contents at the ileo-cæcal junction ; that is, the approximate normality of the small intestine as compared with the almost completely dry condition of the cæcum and large bowel.

The spastic condition of the *Anal Sphincter* is obvious on rectal examination of the patient.

On *post-mortem* examination no definite structural change has been described as constant. The distension of the stomach with fluid and the sharp change which occurs in the gut at the ileo-cæcal junction have already been mentioned. The symptom of regurgitation may fairly be regarded as a secondary effect dependant upon the gastric distension.

It will be seen that the symptoms of acute grass disease appear to be wholly referable to functional disorder, in that they develop without appreciable cause, and cannot be associated with any recognisable organic lesion.

Now, let us compare the effects produced by sympathetic stimulation with the symptoms of acute grass disease.

TABLE No. 2.

Effects of Sympathetic Stimulation.		Symptoms of Acute Grass Disease.
Dilated	Pupil	Normal
Accelerated	Heart	Accelerated
Salivation ; (thick and glairy)	Salivary Glands	Salivation ; (thick and glairy)
Inhibition	Stomach	Stasis
Constriction	Pyloric Sphincter	Constriction
Inhibition	Intestines	Stasis
Constriction	Ileo-Cæcal Sphincter	Constriction
Relaxation	Bladder	Frequently retention of urine
Secretion	Sweat Glands	Sweating
Tremor	Superficial Muscle	Tremor
Increased plastic tonicity	Voluntary muscle	" Resistance " to palpation
Relaxation	Bronchi	*Unknown*
Constriction	Anal Sphincter	Constriction

It will be observed that a comparison of the symptoms of acute grass disease with those of Sympathicotonia presents a remarkable similarity ; indeed the similarity is so close as to appear beyond the possibility of chance. The one exception would seem to be provided by the pupil. Some observers have stated that the pupil was dilated in

Acute Grass Disease, but careful examination of a number of cases would indicate that the pupil is approximately normal.

It has been generally believed that sympathetic stimulation, induced by the intravenous injection of adrenaline, caused appreciable dilatation of the pupil in the horse. This does not agree with the few observations I have made on the point in the course of practice, and through the kindness of Professor Pool and his assistant Mr. Brownlee, facilities were recently given me to put the matter to the test of experiment.

The pupils of three horses were carefully measured, and thereafter a solution of adrenaline chloride, 1 in 10,000 in doses of 40, 50 and 60 c.c. was administered intravenously to each horse respectively. In each case an intense sympathicotonia was developed, but in no case was there any appreciable change in the pupil. By way of comparison, after an interval of forty-eight hours, one of the test horses was given $\frac{1}{2}$ gr. atropine sulphate intravenously ; a pronounced mydriasis developed within a few minutes, and the pupil remained dilated for several hours.

Professor A. J. Clark, of Edinburgh, and Professor Pool, obtained similar results in two cases, in that they observed that the sympathicotonia consequent upon intravenous injection of adrenaline, although evidenced by pronounced cardiac acceleration, rise in blood pressure, sweating, tremor, etc., elicited no perceptible effect upon the pupil.

It would seem then, that (in contradiction to established belief) the pupil of the horse does not appreciably respond by dilatation to the sympathetic stimulation induced by adrenaline. On the other hand dilatation is readily induced by parasympathetic depression.

The normality of the pupil in grass disease may therefore be regarded as the exception which goes to prove the rule.

While my interpretation of acute grass disease as a Sympathicotonia may be admitted, it may also be argued that the condition is a relative, and not an absolute one, *i.e.*, that it arises from a depression of the Parasympathetics rather than from a stimulation of the Sympathetics.

On reference to Table No. 1, it will be seen that certain structures are innervated by the Sympathetic only, *e.g.*, the intestinal sphincters and the sweat glands. Now, if

an *absolute* depression of the Parasympathetics occurred in grass disease, these structures would not be activated. The experiments referred to above in which the pupil dilated to Parasympathetic depression and not to Sympathetic stimulation would appear to lend further support to this view.

In this connection it seems to me that the height of blood pressure and the degree of sugar tolerance which obtain in grass disease should be determined.

If, then, as appears to be the case, the symptoms can be interpreted as representing an excessive stimulation of the sympathetic system, one is led to enquire what type of factor is capable of producing such stimulation.

We know that the normal stimulation of the sympathetic in health is largely maintained by the adrenal medulla, and with this endocrine gland the thyroid is believed to co-operate. It is probable that the symptoms arise from overactivation of this group ; but this overactivation must in turn, be dependant upon some primary factor. That such factor is of exogenous origin is clearly shown by the well known geographical distribution of the disease

(*a*) *Poisonous Plants* : At least one plant, *Ephedra vulgaris*, is known to produce a substance, Ephedrine, which elicits powerful sympathetic stimulation. The plant is not, however, a native of this country. The possible connection between the disease and plant poisoning has been, hitherto, necessarily conducted in a somewhat desultory manner. A thorough systematic enquiry seems highly desirable.

(*b*) *Fungi* : Ergot contains certain active substances, such as Ergotoxin and Tyramine which are sympathetic stimulants. It is not suggested that Ergotism is necessarily related to the disease, but it is possible that other fungal parasites of grass may contain toxins of a similar nature.

(*c*) *Bacterial Toxins* : So far as one is aware no bacterial toxin is known to be a specific sympathetic stimulant, although the symptoms of botulinus intoxication bear some resemblance to grass disease, and the pharmacology of the botulinus group of toxins requires investigation.

(*d*) *Parasital Toxins*: No protozoal or other parasital toxin of animal origin is at present known to possess this action.

(*e*) *Sympathi-mimetic Amines*: As the result of liver disfunction certain amino bases, notably Tyramine and Phenyl-ethyl-amine, may be liberated in the imperfect breakdown of their respective amino-acids. They produce the effect of sympathetic stimulation (sympathi-mimetic), and, although their action is less powerful than that of adrenaline, it seems possible that their continued action may produce the sympathicotonia of grass disease. If this be so it postulates a specific primary toxin or animate virus which is capable of hindering the normal deaminization of these toxic metabolites in the liver.

A histological study of the liver in acute grass disease, therefore suggests itself.

In offering this attempt to interpret the symptoms of acute grass disease, I confess I do so with some reluctance; but our knowledge of the pathogenesis of the disease is still so meagre that the expression of any fresh view usually meets with some measure of consideration. I therefore present these tentative opinions in the hope that if they do not help in suggesting a clue to the etiology, they may, perhaps, lead to a clearer understanding of the nature of the disease.